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It is a common belief that people tend to gain weight on stopping smoking. For fear of gaining weight they may continue to smoke and thus retain a significant risk factor for cardiovascular and pulmonary disease. We have studied 4 lean young men who habitually smoked a pack of cigarettes a day. Food intake was kept constant throughout the study, which incorporated periods of smoking and non-smoking in an on-off-on design. The relative importance of change in hunger, in hormonal responses, plasma substrate concentrations, appetite and metabolic rate were thus assessed

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EFFECTS OF CIGARETTE SMOKING ON BODY WEIGHT, ENERGY EXPENDITURE, APPETITE, AND ENDOCRINE FUNCTION

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Running Title: (Cigarette) Smoking, Weight, Appetite, and Endocrine Function

ABSTRACT

It is a common belief that people tend to gain weight on stopping smoking. For fear of gaining weight they may continue to smoke and thus retain a significant risk factor for cardiovascular and pulmonary disease. We have studied 4 lean young men who habitually smoked a pack of cigarettes a day. Food intake was kept constant throughout the study, which incorporated periods of smoking and non-smoking in an on-off-on design. The relative importance of change in hunger, in hormonal responses, plasma substrate concentrations, appetite and metabolic rate were thus assessed independently of change in caloric intake.

Only small, statistically insignificant fluctuations in weight occurred during the course of the study. In 3 of 4 subjects, weight was increased during the period of non-smoking by 0.9 kg and decreased after resumption of smoking by 1.2 kg. During standardized walking exercise in the non-smoking period, the heart rate was significantly lower than during the periods of smoking. There were no changes in resting or walking metabolic rate observed to support any significant decrease in energy expenditure during the non-smoking period. Appetite ratings nearly doubled ($p < 0.01$) at that time, however. The TSH response to TRH was significantly suppressed during the two periods of smoking, which may reflect a central effect of smoking; the response of prolactin to TRH was not affected. The changes in concentrations of TSH, T_4, or T_3 were not significant, although the direction of change in each subject at the end of each period, together with the small weight change, raised the possibility of a slight increase in thyroid activity. It can be concluded, however, that the most potent mechanism for the promotion of weight gain on stopping smoking is the release of appetite from suppression.

Because of the large number of anecdotal reports of undesired weight gain after quitting smoking, the folklore that ceasing to smoke causes weight gain has achieved the status of belief. Because of this belief and their own experience, or that of others, many people continue to smoke. This represents a poor tradeoff, since the risk factors for cardiovascular and pulmonary disease from smoking are added to the other risk factors. In the Evans County survey, Heyden et al. (1) found that overweight was a risk factor for coronary disease in smokers, but not in non-smokers.

Brozek and Keys (2) documented the gains in weight in a group of professional men studied over five years and established that those who had stopped smoking gained more weight. The relationship is neither constant nor simple, however. In the Framingham study, Gordon et al. (3) found a weight increase in men, but not in women who had stopped smoking, but it was relatively short-lived. Bosse et al. (4) found that younger, leaner, more frequent smokers tended to gain more weight after quitting and that 36 percent of their subjects either did not gain or actually lost. Ashwell and North (5) have found that, at least in England, social class also must be taken into consideration. Upper class male smokers were heavier than non-smokers, whereas in lower social classes the reverse was true. Among women the only significant difference was within the lower classes. Jacobs and Gottenborg (6) have analyzed weight in relation to smoking status, age, and sex, and self-perceived relative physical activity in a randomly selected population of 1557 subjects. They found that smokers of 15-29 cigarettes per day consumed at least as many or more calories as those who never smoked and yet had lower weight.

The many possible effects of smoking upon food intake, body weight, and energy expenditure have been extensively reviewed by Mack and Rodin (7). To date the mechanisms remain incompletely clarified. Some years ago Batterman (8) suggested that inhibition of gastric "hunger" contractions explained the slimness of some smokers. Recently, attention has centered on the effects of nicotine on the central nervous system, particularly the hypothalamus, with focus on neurotransmitters and endocrine function. We are not aware, however, of any studies that have directly investigated the role of nicotine centrally on any of the processes of body weight maintenance. In one frequently cited study (9) it was claimed that gain in weight one month after cessation of smoking was due to decreases in metabolic rate and protein-bound iodine, and heart rate. In the present study diet was kept constant in both caloric content and composition and an on-off-on design was employed to evaluate the independent effects of smoking or not smoking on appetite, energy expenditure, body weight and selected endocrine functions.

METHODS AND RESULTS

Experimental Subjects

Experimental subjects were four paid volunteers, two medical students and two hospital employees of mean absolute weight 70.5 ± 3.4 (SD) kg. Their relevant physical characteristics are shown in Table 1. Three of the four subjects were selected for their previous tendency to gain weight. Subjects 2 and 3 had previously gained weight after temporarily quitting smoking; subjects 3 and 4 had previously been overweight by 22-24.5 kg. Each had smoked 1-1.5 packs a day of common brands of cigarettes for the past 4-8 years. All drank from 3 to 5 cups of coffee per day throughout the study.

None drank alcoholic beverages during the study. All signed statements of informed consent, after receiving a detailed explanation of the procedures and risks involved and their right to withdraw at any time without prejudice.

Experimental Design

During an 11-day control period (smoking control, SC period), the subjects smoked their usual pack a day of cigarettes while taking a diet of controlled composition (45% carbohydrate, 15% protein, and 40% fat) provided by the Clinical Research Center. Caloric content was adjusted as necessary so that each individual could maintain his usual weight during this period. The meals were prepared from single lots of pre-packaged frozen meals (Swanson's TV dinners) supplemented as necessary. A fixed quantity of sweets and nuts, to be consumed as snacks during periods of craving upon withdrawal of smoking, were included as a dietary component throughout all periods of the study. At the completion of the 11-day baseline SC period, the subjects completely abstained from smoking while the identical diet was continued for a non-smoking (NS) period of 21 days. This was followed by a second period of resumed normal smoking for 20 days (RS period). Testing was carried out during the final week of each period. The men took all their meals under supervision of the Clinical Research Center staff. They slept in the Center but went about their usual daily routines in the Medical Center, taking their allowed snack foods with them. Thus, they were not continuously isolated or monitored at all times of day, and some reliance was necessarily placed on their being known to the investigators as reliable subjects. Physical activity was maintained constant as far as possible and relative constancy of

physical activity was checked daily by pedometer readings. The number of cigarettes smoked each day was recorded and was maintained constant for each individual, and the body weights were also recorded each morning after voiding.

During the smoking periods, the subjects did not smoke on the mornings on which tests were carried out, and thus any acute, short-term effects of smoking were not observed.

Endocrine and Metabolic Studies

These were carried out during the last 7 days at the end of each of the three periods. Glucose tolerance to 100 gm taken orally was measured over a 5-hour period, with analyses by a glucose-oxidase procedure. Insulin was measured by double-antibody radioimmunoassay (10) and free fatty acids by a modification of the automated method of Novak (11). The response of thyroid stimulating hormone (TSH) and of prolactin to 500 ug of thyrotropin releasing hormone (TRH) given intravenously was measured at 15, 30, 45, 60, 90 and 120 min. TSH, thyroxine (T_4) and total triiodothyronine (T_3) were measured as previously described (12). Prolactin was measured by radioimmunoassay using a modification of the method of Sinha et al. (13), with standards and antigen supplied by the National Pituitary Agency and the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases. The TRH was supplied by the Abbott Company. Luteinizing hormone releasing hormone (LHRH), 250 ug, was given intravenously along with the TRH; and FSH and LH were measured at the same intervals as TSH. Serum total cholesterol and triglycerides were measured by Autoanalyser.

Metabolic and Thermogenic Assessment

At the end of each of the three periods the volunteers were transported by car to the U.S. Army Research Institute of Environmental Medicine, Natick, MA, for measurements of metabolic rate under controlled environmental conditions. The assessments began two hours after lunch on the day of arrival and continued through the following morning. In an environmentally controlled laboratory oxygen consumption (VO_2) and CO_2 production (VCO_2) were measured during every fifth minute of a 15-minute walk on a level treadmill at 5.6 km/hr. Expired breath was collected by open circuit Tissot spirometry and analyzed by Beckman Model E-2 O_2 and LB-2 CO_2 analyzers. The analysers were calibrated every 20 minutes with reference gases previously analyzed by the Scholander micro-technique (14). Metabolic rate was then calculated according to the method of Wier (15). The subjects were also studied 2 hours later while they rested semi-nude on bunks in a chamber with a controlled environment (ambient temperature 27.7 ± 0.5°C, relative humidity 50 ± 5%); body, skin and rectal temperatures were measured every two minutes. Pre- and post-prandial resting metabolic rates were determined every half hour, for one hour before a standard supper containing approximately 1000 kcal distributed as in the maintenance diet and for 4 hours thereafter.

The subjects slept undisturbed overnight in the environmental chamber until 6:00 AM, at which time they were aroused just enough to enable duplicate collections of expired air to be made over a 30-minute period for determination of the awakening resting metabolic rate (RMR). After a period during which the subjects rose, washed, voided and ate a standard breakfast, metabolic measurements were resumed and were continued every half hour for 3.5 hours.

During each of the three experimental periods observations were made within 10 minutes of the same time of day. The same protocol was followed on each occasion, with the exception of the inclusion of a 5-minute period of familiarization with treadmill walking at the start of the first series of studies.

Rating of Appetite

The volunteers rated their degree of appetite before breakfast and before supper each day during the 11 days of the smoking control (SC) period and the last 11 days of the following two (NS and RS) periods. An 11-point scale was used, which was anchored at both ends with zero representing no appetite whatever and 10 the maximal possible craving for food.

Statistical Analyses

Repeated measures treatment-by-subjects analysis of variance (16) was used for testing group mean values at a significance level of $p < 0.05$. These were followed by Tukey honestly significant difference post hoc comparisons when warranted (17). In evaluating the stimulation tests, the concentrations of the responding hormones were multiplied by their appropriate time intervals to give a time-weighted "area" under the curve. Unless otherwise indicated, means and standard errors are reported.

RESULTS

Changes in Body Weight

During the control (SC) period, caloric intake was adjusted at intervals to maintain the subjects' weight, which became stable during the last week of the period. Therefore, the individual weights from only the last 5 days of

each period were incorporated into the analysis of variance for comparison of mean body weight across experimental periods. End-of-period weights averaged 70.5 ± 1.7 kg (SC), 71.4 ± 1.8 (NS); and 70.6 ± 2.0 (RS). These differences did not reach significance ($0.05 < p < 0.10$). Individual results are shown in Table 1.

Appetite Ratings

One of the three positive changes noted in the study was related to appetite. Relatively low levels of appetite were recorded during the control periods; when abstaining from smoking, however, the volunteers were hungry and had increased tolerance for the TV dinners. Their appetite ratings, assessed in terms of the rating scale just before the morning and evening meals are shown in Figure 1. During the last 7 days of the first control period, ratings for supper (TV dinner) fluctuated slightly about an average of 2.6 and for a breakfast freshly prepared in the Clinical Research Center about an average of 4.0. Over the first 9 days of the NS period, appetite for both meals increased progressively and at similar rates. By the 10th day a peak rating of 6.8 - 7.0 was reached with subsequent decline to 6.0, significantly above the NS ratings ($p < 0.01$). On the first day that smoking was resumed, hunger was substantially depressed (before breakfast 3.8, before supper 3.2) but not to baseline values. Within 4-5 days appetite for supper recovered slightly to a peak of 4.5. Thereafter, until the end of the study, appetite declined slowly to reach final ratings of 2.5 for breakfast and 3.5 for supper, both significantly less than the values at the end of the NS period ($p < 0.01$), but not significantly different from the corresponding ratings at the end of the SC period.

Metabolic Rate on Awakening and During Exercise

There were no significant changes in resting metabolic rate upon awakening. Similarly, there were no detectable changes in the responses of oxygen consumption, respiratory quotient, and metabolic rate during level walking at 5.6 km/hr on the last day of each of the three periods.

Cardiac Response to Exercise

Resting heart rates did not differ significantly during the three periods. There were, however, significant differences when walking (Table 3). During the NS period, the heart rate was significantly lower than during the SC period by 14 ± 3 beats per minute ($p < 0.05$) and was marginally lower during the period of resumption of smoking by 6 ± 2 beats per minute ($p = 0.05$).

Metabolic Rates and Body Temperature in Relation to Meals

The resting metabolic rates before and after supper and breakfast are shown in Figure 2. Analysis of variance showed no significant differences across periods between any of the metabolic rates. The postprandial rise and fall after the larger evening meal is readily apparent, but there was no indication of association with smoking status. Although not illustrated, the body core and skin temperatures showed the typical circadian pattern, with no significant differences related to smoking.

Fasting Concentrations of Substrates

Fasting glucose concentrations were essentially identical during the three periods of the experiment. Mean fasting serum levels of free fatty acids, triglycerides, cholesterol, insulin, glucagon, and growth hormone also

were not significantly different. The glycemic and hormonal response to 100 gm of oral glucose and the decrease in free fatty acids did not differ during the three periods either.

Fasting Concentrations of Thyroid Hormones and Response of TSH and Prolactin to TRH Stimulation

The response curve of TSH to TRH (Fig. 3) was significantly higher during the NS period than during either of the smoking control periods ($p < 0.01$, Table 4). Consistent with the increased TSH response to TRH, the serum concentrations of T_4, T_3, and of TSH all changed slightly during the non-smoking period in the direction of decreased thyroid function and rebounded on resumption of smoking, but the changes were far from significant(Table 4). In contrast, there were no changes in the response of prolactin to TRH, however (Fig. 3).

Fasting Gonadotropin and Serum Testosterone Concentrations and the Response to LHRH Stimulation

There was no consistent pattern of change in the concentrations in the serum of FSH, LH or of testosterone before stimulation with respect to periods of smoking and of non-smoking. The NS response of FSH to LHRH was significantly higher ($p < 0.05$) than the SC value, but did not decline significantly upon resumption of smoking. The fasting concentration of testosterone in the serum and its response to LHRH by 240 minutes did not differ significantly in any of the periods.

DISCUSSION

The present study is concerned with both lean and formerly obese young men smoking a pack or more of cigarettes a day of common brands. It is the first human or animal study of the effects of smoking or of nicotine in which intake of food has been kept constant, so that the relative importance of changes in appetite and energy expenditure could be assessed separately from a change in caloric intake. Thus, any observed changes in hormonal response or in substrate concentrations could not be attributed to dietary effects. Since the hormonal studies were all carried out 10 hours after the last cigarette of the day, immediate effects of smoking were not investigated.

If a relative decrease in metabolic rate between the non-smoking and smoking periods were the predominant mechanism of the weight gain after stopping smoking, one would expect a gain during the period of abstinence followed by a drop on resumption. Although there was individual variation in the timing and degree of weight gain, the final weights of three of four of the volunteers held to this pattern (Table 1); however, their total gain over three weeks averaged less than a kilogram. The metabolic rates on awakening or during standardized walking did not vary significantly.

One of the three definitely positive results of the present study was the contrast between the lesser response of TSH to TRH stimulation in the smoking vs the non-smoking periods. Since the usual response of prolactin to the same stimulus was not reduced, this was all the more striking. The degree of TSH response of our four subjects during their non-smoking periods was within the range of normal for non-smokers as determined in our laboratory (12), and thus it appears that the TSH response was depressed during smoking. An increased

response of TSH to TRH is usually associated with hypothyroidism and a decrease with hyperthyroidism, but there are a number of exceptions to this, such as the responses in depression, cortisol excess, and aging. However, the possibility that smoking directly stimulates thyroid function should not be dismissed on the basis of the present findings in this limited number of moderate smokers. The trends in the four parameters of thyroid hormone activity, although small, were all consistently in the direction of increased primary thyroid activity during the periods of smoking and these changes are consistent among the four subjects. These include increased T_4 and total T_3, decreased TSH, and decreased TSH response to TRH. These, although not statistically significant by themselves, together with the change in weight, suggest that further study of thyroid function, catecholamine response, and the rate of energy expenditure is indicated. Dalloso and James (19) have recently suggested that decreased thermogenesis as well as increased food intake may account for increased weight gain in reformed smokers. They found that, of 10 such subjects, six had an increase in spontaneous intake of food while 5 had a decrease in resting metabolic rate measured by the ventilated hood technique. Smoking a single cigarette increased the resting metabolic rate.

It is also possible that smoking in some manner diminishes the TSH response through a direct or indirect effect of nicotine or other constituent of cigarette smoke within the central nervous system, perhaps on the hypothalamic releasing and inhibiting mechanisms and the pituitary. Sorting out the possible effects of nicotine itself on the central nervous system is complicated by the recent finding of Rowe et al. (18) that nicotine given intravenously has no effect on vasopressin secretion, whereas comparable

amounts given by inhalation are effective. The drug raises pulse rate and blood pressure by either route. Apparently the same dissociation with respect to route of administration of nicotine may apply to its effect on growth hormone as well. While inhalation of cigarette smoke in man gives a brisk rise in growth hormone (20), intravenous injection of nicotine in small doses inhibits growth hormone secretion (21). Studies of the effect of nicotine on the central nervous system in animals have of necessity involved indirect methods such as intrathecal injection in vivo, or in vitro studies of tissue slices. The CNS effects of nicotine have been reviewed through 1961 by Silvette et al. (22) but provide little information on possible mechanisms affecting metabolism. A recent study by Andersson et al. (23) offers a possible mechanism whereby nicotine can inhibit the secretion of TSH. Using the catecholamine ganglionic blocking agent mecamylamine, they blocked nicotine's ability to inhibit TSH and gonadotropin secretion. They suggest that nicotine initially stimulates a cholinergic nicotinic receptor which stimulates dopamine, norepinephrine and epinephrine terminals within the hypothalamus and that the actions of the released catecholamines, in turn, inhibit secretion of the tropic hormones. The recent studies of Yoshida et al. (24) have also demonstrated nicotine-induced release of norepinephrine from synaptosomes of the rat in vitro. In Andersson's experiments, secretion of epinephrine was also blocked by nicotine. It is not clear why prolactin secretion was not suppressed along with TSH in the present experiments.

Glauser et al. (9) concluded from a study of regular smokers not consuming a controlled diet that the increase in noted weight 4 weeks after stopping smoking was a result of significantly reduced resting metabolic rates. Recalculation of two-tailed Student's t-test of paired values from the data in that

report failed to confirm the reported significance at $p < 0.05$ of the change in several important variables after smoking was stopped: body weight ($0.05 < , p < 0.1$), oxygen consumption ($p > 0.1$), RQ ($0.05 <, p < 0.1$), heart rate ($p > 0.1$) and protein-bound iodine ($p > 0.1$) but did confirm the significance of the reported changes in serum calcium level and 30-min minus fasting blood glucose levels. Since the fundamental conclusion of the report was in doubt, we computed resting metabolic rate from the VO_2 and VCO_2 data in the report by Weir's non-protein method (15), and found the averages to not differ significantly by t-test ($p > 0.1$): 46.4 ± 1.4 (SE) and 42.5 ± 1.7 W/m^2 for the smoking and the non-smoking states, respectively. Thus, the data from the earlier report appear to be in agreement with our finding that neither resting oxygen consumption nor metabolic rate changes significantly after smoking is stopped.

The second clear-cut, positive finding of the present study was the enhancement of appetite during the period of abstinence. The procession of TV dinners, monotonously cycled in the three periods to achieve uniformity, was far from a gourmet experience for the volunteers. After the first several days of not smoking, however, they developed hunger to such a extent that they said that they would welcome the opportunity to eat several of the TV dinners at a single sitting, as the appetite ratings of Figure 1 might suggest. Further experiments would be required to determine whether certain types of individuals may be more susceptible to hunger under such conditions and to determine how long the increased hunger might persist after smoking has been stopped. It is possible that, since the subjects worked as a group, their subjective reactions may also have been influenced by other members of the group, but the extent to which their appetite ratings increased exceeded any

expected effect from this cause. The mechanism of the increased hunger is not clear; whether there may be a common mechanism underlying the suppression of TSH release and of appetite can only be conjectured. Electroencephalographic and other studies (7,21) indicate that nicotine is a CNS stimulant in low dosage and a depressant in higher dosage. The former effect might be expected to enhance food intake. In the intact rat, however, both amphetamine and nicotine depress food intake when given subcutaneously, but there is no cross tolerance and different mechanisms appear to be involved (25). Again, it is possible that other constituents of cigarette smoke may have been responsible for the observed effects.

Further studies will be needed to clarify the mechanisms of the increased appetite which occurs on stopping smoking. With such knowledge it may be possible to provide better counsel to those who would like to avoid the cardiovascular and other risk factors of smoking and also to avoid the penalty of weight gain. Such studies should include both the acute and the chronic effects of smoking on energy balance. The possibilities of direct or indirect effects of smoking on secretion of thyroid hormones should also be investigated.

In conclusion, it appears from this study that the most potent mechanism promoting weight gain on stopping smoking is the removal of the suppression of appetite. We have not completely excluded a slightly increased metabolic rate brought about by increased thyroid or catecholamine hormonal activity as a contributory factor to limitation of weight gain while smoking.

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The views opinions, and/or findings contained in this report are those of the authors and should not be construed as an official depeartment of the Army position, policy, or decision, unless so designated by other official documentation.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

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Table 1. Subject Age, Height, Previous Maximum Weight, Dietary Intake, Anthropometric Variables, Body Weight and Resting Heart Rate throughout the Study.

Subject	Age (yr)	Height (cm)	Previous Maximum Weight kg	Dietary Intake (kcal/d)	Weight at End of Period (kg)			Heart Rate (beat/min)		
					SC	NS	RS	SC	NS	RS
1	23	167	70.5	3220	69.8	70.7	69.9	78	72	74
2	23	181	80.9	3470	74.6	75.6	75.7	60	62	56
3	27	184	93.2	3100	71.2	72.7	70.8	64	60	67
4	25	166	90.9	2450	66.4	66.8	65.8	66	56	59
Mean					70.5	71.4	70.6	67.0	62.5	64.0
S.E.					1.7	1.8	2.0	3.9 3.9	3.4 3.4	4.1 4.1

Periods are SC = Smoking Control, NS = Non-smoking, and RS = Resumption of Smoking.
The weight was averaged from the last 5 days of each period.

Table 2. Resting Metabolic Rate on Awakening and During Level Walking at 5.6 km/hr

	On Awakening			During Level Walking							
	Metabolic Rate (W/m^2)			Metabolic Rate (W/m^2)			RQ				
Subject	SC	NS	RS	SC	NS	NS	RS	RS	SC	SC	NS	NS	RS	RS
1	49	43	38	228	220		230		0.84		0.89		0.90	
2	41	40	45	212	210		206		0.89		0.85		0.87	
3	51	49	46	199	199		192		0.74		0.78		0.83	
4	59	52	49	216	198		211		0.84		1.03		1.01	
Mean	50.2	46.0	44.5	213.8	206.8		209.7		0.83		0.89		0.90	
S.E.	3.7	2.7	2.3	6.1	5.1		7.8		0.03		0.05		0.04	

SC = Smoking Control Period. NS = after 3 weeks of Not Smoking.

RS = 3 Weeks after Resumption of Smoking.

No differences statistically significant ($p > 0.1$)

Table 3. Mean Cardiorespiratory Responses During Level Walking at 5.6 km/hr

	SC	NS	RS
Heart Rate b/min	115.8 ± 6.7	101.5* ± 6.4	106.5* ± 5.4
Respiratory Rate f/min	17.8 ± 2.6	19.8 ± 0.6	19.5 ± 1.0
V_E (l/min BTPS)	27.1 ± 2.0	28.3 ± 1.6	27.3 ± 1.8

SC = Smoking Control Period, NS = After 3 Weeks of Not Smoking, RS = 3 Weeks after Resumption of Smoking.

* SC vs. NS $p < 0.05$; NS vs RS, ($p = 0.05$). No other differences were significant.

Table 4. Thyroid Hormone Concentrations and Response to Thryotropic Releasing Hormone

TEST	SC	NS	RS
THYROID HORMONE CONCENTRATIONS			
Thyroxine (g/dl)	4.14 ± 0.65	4.08 ± 0.49	4.60 ± 0.32
Triiodothyronine (ng/dl)	139 ± 10	133 ± 7	144 ± 8
THYROID RELEASING HORMONE STIMULATION			
Thyroid Stimulating Hormone (uIU/ml)*			
0 minutes	1.1 ± 0.39	1.7 ± 0.44	1.2 ± 0.42
Sum 15-120 minutes**	55 ± 17	82 ± 19	52 ± 17
Prolactin			
0 minutes	8.0 ± 0.8	7.5 ± 1.5	9.0 ± 0.9
Sum 15-120 minutes	125 ± 16	131 ± 18	135 ± 19

* Values less than 1 taken as 1

** NS > SC & NS > RS: $p < 0.01$. HSD = 22.7 [Honestly Significant Differences, Tukey (17)]

All other differences not significant.

Figure Legends

Figure 1. Mean ratings (± SE) of 4 subjects for appetite prior to breakfast and supper each day. Ratings during the non-smoking period were significantly greater for both breakfast and supper ($p < 0.01$). Smoking control and resumption periods not statistically different ($p < 0.10$).

Figure 2. Pre- and post-prandial resting metabolic rates. Averages of 4 subjects. S E indicated by shading. No differences were significant ($p > 0.20$).

Figure 3. Response of Thyroid Stimulating Hormone and of Prolactin to stimulation with Thyrotropin Releasing Hormone (N = 4). See Table 5 for integrated responses and statistical significance.

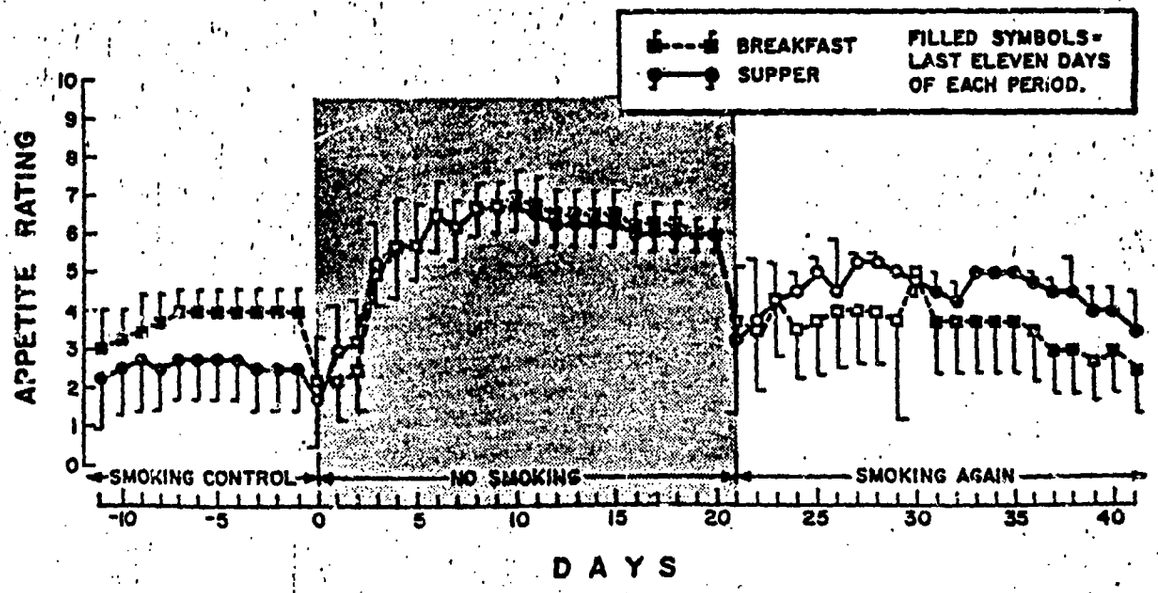
BREAKFAST
SUPPER
FILLED SYMBOLS = LAST ELEVEN DAYS OF EACH PERIOD.
APPETITE RATING
0
1
2
3
4
5
6
7
8
9
10
SMOKING CONTROL
NO SMOKING
SMOKING AGAIN
-10
-5
0
5
10
15
20
25
30
35
40
DAYS

FIGURE 1

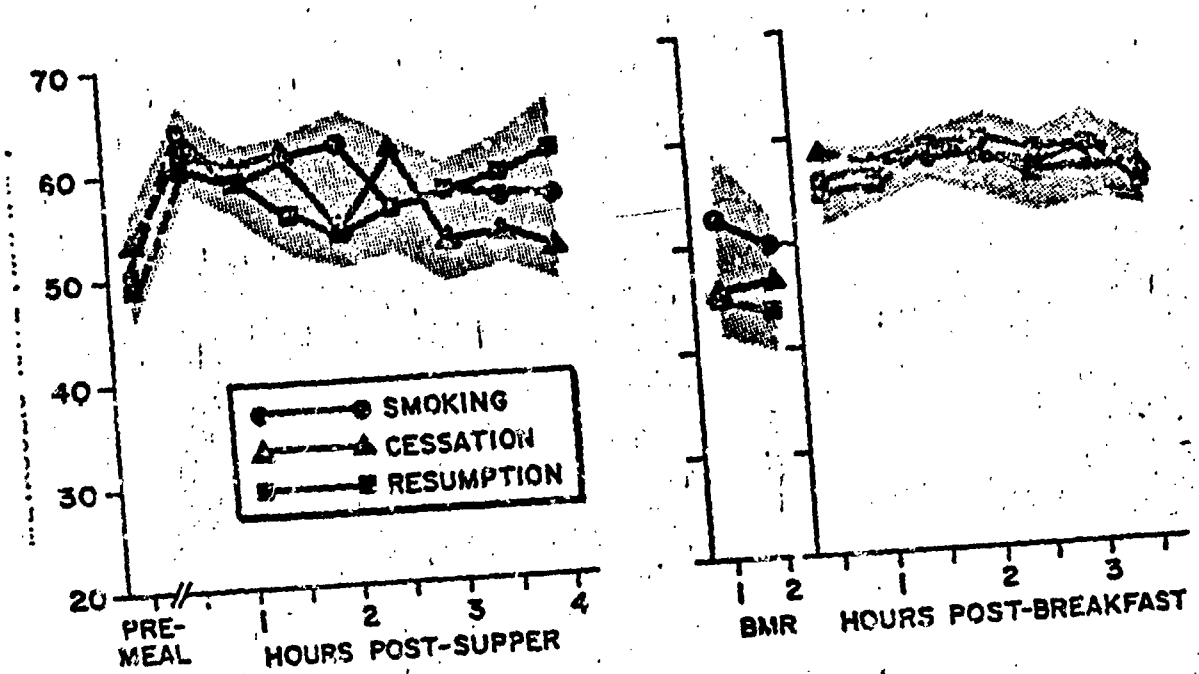
70
60
50
40
30
20
SMOKING
CESSATION
RESUMPTION
PRE-MEAL
1
2
3
4
HOURS POST-SUPPER
BMR
1
2
1
2
3
HOURS POST-BREAKFAST

FIGURE 2

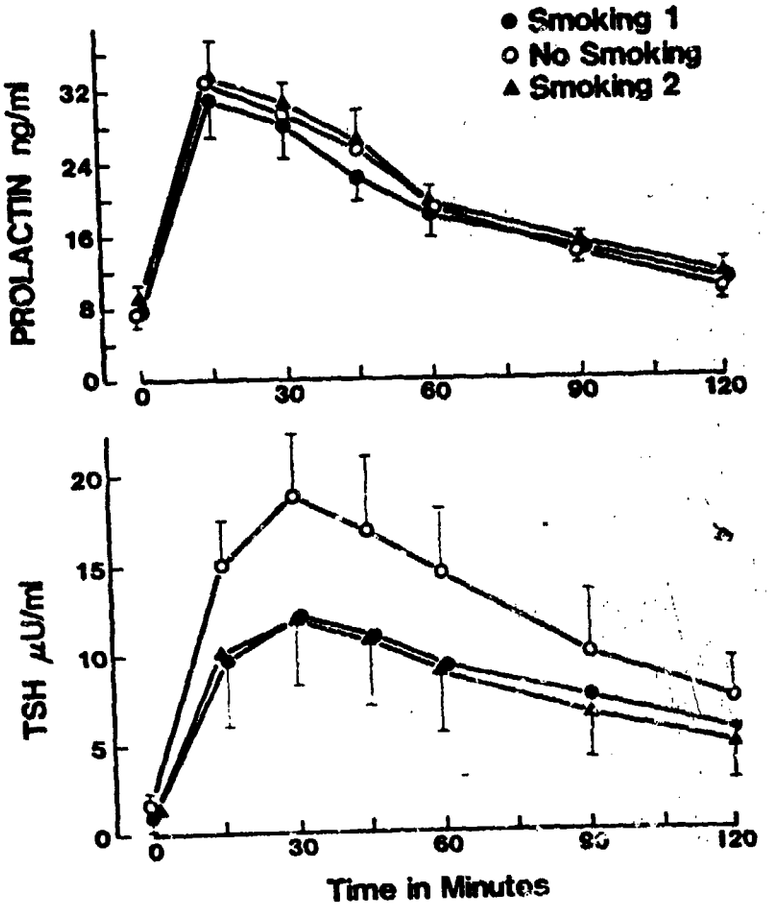
● Smoking 1
○ No Smoking
▲ Smoking 2
PROLACTIN ng/ml
32
24
16
8
0
0
30
60
90
120
TSH μU/ml
20
15
10
5
0
0
30
60
120
Time in Minutes

FIGURE 3